

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
16 June 2005 (16.06.2005)

PCT

(10) International Publication Number
WO 2005/054814 A1

(51) International Patent Classification⁷: G01N 1/30, (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(21) International Application Number: PCT/US2004/039650

(22) International Filing Date: 26 November 2004 (26.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 60/525,220 26 November 2003 (26.11.2003) US

(71) Applicant (for all designated States except US): YALE UNIVERSITY [US/US]; 433 Temple Street, New Haven, CT 06511 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): MOR, Guillermo [US/US]; Two Whitney Avenue, New Haven, CT 06511 (US).

(74) Agents: ZISKA, Suzanne, E. et al.; Morgan, Lewis & Bockius LLP, 1111 Pennsylvania Avenue, NW, Washington, DC 20004 (US).

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/054814 A1

(54) Title: APOPTOSIS-BASED EVALUATION OF CHEMOSENSITIVITY IN CANCER PATIENTS

(57) Abstract: Induction of apoptosis in target cells is a key mechanism by which chemotherapy induces cell killing. An *in vitro* system has been established for determining carboplatin and paclitaxel (Taxol) chemosensitivity of epithelial ovarian cancer cells, where measurements of caspase-3 activation are surrogate markers for activation of chemotherapy-induced programmed cell death. To validate the assay as a predictor of clinical chemotherapy-induced programmed cell death. To validate the assay as a predictor of clinical chemosensitivity *in vitro* apoptotic response were compared to the clinical response of the patients from whom the tumor cells were isolated. Caspase-3 activation in response to *in vitro* chemotherapy to both drugs was shown to have an 83 % positive predictive value and a 71 % negative predictive value. Markers of apoptosis such as caspase-3 activation can be quantitated and utilized to predict the clinical response to chemotherapy.